Citation:

Key TJ, Appleby PN, Spencer EA, Travis RC, Roddam AW, Allen NE. Cancer incidence in vegetarians: Results from the European Prospective Investigation into Cancer and Nutrition (EPIC-Oxford). *Am J Clin Nutr*. 2009 May; 89(5): 1,620S-1,626S. Epub 2009 Mar 11.

PubMed ID: 19279082

Study Design:

Prospective Cohort Study

Class:

B - Click here for explanation of classification scheme.

Research Design and Implementation Rating:

POSITIVE: See Research Design and Implementation Criteria Checklist below.

Research Purpose:

To examine cancer incidence among vegetarians and non-vegetarians in the European Prospective Investigation into Cancer and Nutrition–Oxford (EPIC-Oxford) study.

Inclusion Criteria:

The analyses were restricted to participants aged 20 to 89 years at recruitment with known smoking characteristics and for whom diet group was unambiguous.

Exclusion Criteria:

History of cancer at baseline (except non-melanoma skin cancer).

Description of Study Protocol:

Recruitment

- The EPIC-Oxford cohort was recruited between 1993 and 1999. Two methods of recruitment were used: General practice (GP) recruitment and postal recruitment
- EPIC nurses working in GP offices performed recruitment from the general population through GPs. All men and women aged 35 to 69 years on the list of each collaborating GP were invited to participate. In addition, a pilot recruitment phase was conducted by collaborating GPs who recruited 900 women aged 40 to 59 years. The GP method recruited 7,423 participants
- Postal recruitment, aimed at those aged 20 years, was designed to recruit as many vegetarians and vegans as possible. The main questionnaire was mailed directly to all members of the Vegetarian Society of the United Kingdom and all surviving participants in the Oxford Vegetarian Study. Respondents were invited to give names and addresses of relatives and friends who might also be interested in receiving a questionnaire. In addition, a short questionnaire was distributed to all members of the Vegan Society, enclosed in health- or diet-interest magazines and displayed on counters of health food shops. The postal methods recruited 58,042 participants.

Design

- This was a prospective study of 63,550 men and women recruited throughout the United Kingdom in the 1990s
- The EPIC-Oxford cohort is one component of the EPIC, a collaborative study of 500,000 men and women in 10 European countries.

Dietary Intake/Dietary Assessment Methodology

- Participants were categorized into one of four diet groups according to their replies to four questions: Do you eat meat? Do you eat fish? Do you eat dairy products? Do you eat eggs?
- For each of these four questions, participants were asked to reply yes or no, and, if they replied no, to record their age when

they last ate the food group concerned. From these four questions, four diet groups were established: meat eaters (those that eat meat), fish eaters (those that do not eat meat but do eat fish), vegetarians (those that do not eat meat or fish but do eat dairy products or eggs or both) and vegans (those that eat no animal products). Because of the small number of cancers among vegans, in this article the vegans are included in the vegetarian category
- For the women recruited in the pilot phase of the study, and the first 1,300 men and women recruited by EPIC nurses, these four dietary categorization questions were not asked, and diet group was assigned according to responses provided in the FFQ (described next)
- Participants completed a FFQ, based on that used in the US Nurses' Health Study, modified for use in the United Kingdom. Each participant estimated his or her average frequency of intake of 130 foods and drinks over the previous 12 months: never, one time per month, one to three times per month, one time a week, two to four times a week, five to six times a week, one time per day, two to three times per day, four to five times per day or six times per day. Daily mean nutrient intakes were then estimated.

Statistical Analysis

- Standardized incidence ratios (SIRs) of vegetarians and non-vegetarians were calculated from incident cancers before age 90 by comparison with contemporary cancer incidence data for England; the SIR is the ratio of the observed number of cancers to the number of cancers expected from the national rates, standardized for age and sex and expressed as a percentage
- Cox regression was used to calculate incidence rate ratios (IRRs) for cancers of the colorectum, female breast, prostate, ovary, lung and all malignant neoplasms combined, comparing cancer incidence rates among participants with no prior malignant cancer for various factors, including diet group
- Analyses were stratified by sex when appropriate, rather than adjusting for this variable. The analyses were thus stratified by sex and method of recruitment and adjusted for smoking, with age as the underlying time variable. Smoking was categorized as never smoker, former smoker, light smoker, or heavy smoker; heavy smokers were those smoking 15 cigarettes per day; light smokers were all other current smokers, including pipe or cigar smokers; and never smokers were those who have never smoked one cigarettes per day for one year.
- Statistical significance was set at the 5% level, and 95% CIs were calculated for both the SIRs and IRRs.

Data Collection Summary:

Timing of Measurements

Recruitment 1993 to 1999; follow-up through December 31, 2005.

Dependent Variables

Cancer incidence: Followed through nationwide cancer registries.

Independent Variables

- Vegetarian status
- Non-vegetarian status.

Control Variables

- Age
- Sex
- Smoking.

Description of Actual Data Sample:

- *Initial N:* 63, 550
- *Attrition (final N):* 52,706
- *Age:* 20 to 89 years
- *Anthropometrics:* Median BMI (kg/m^2) =
  - Men: Non-vegetarians = 24.3; Vegetarians = 22.9
  - Women: Non-vegetarians = 23.1; Vegetarians = 22.0
- Location: United Kingdom.

Summary of Results:

Key Findings

- The standardized incidence ratio for all malignant neoplasms for all participants was 72% (95% CI: 69%, 75%)

- The standardized incidence ratios for colorectal cancer were 84% (95% CI: 73%, 95%) among non-vegetarians and 102% (95% CI: 80%, 129%) among vegetarians
- In a comparison of vegetarians with meat eaters and after adjustment for age, sex and smoking, the incidence rate ratio for all malignant neoplasms was 0.89 (95% CI: 0.80, 1.00). The incidence rate ratio for colorectal cancer in vegetarians compared with meat eaters was 1.39 (95% CI: 1.01, 1.91).

	Colorectal Cancer		Female Breast Cancer		Prostate Cancer		Ovarian Cancer		Lung Cancer		All Malignant Neoplasms	
	No. of Incident Cancer	IRR (95% CI)	No. of Incident Cancer	IRR (95% CI)	No. of Incident Cancer	IRR (95% CI)	No. of Incident Cancer	IRR (95% CI)	No. of Incident Cancer	IRR (95% CI)	No. of Incident Cancer	IRR (95% CI)
Vegetarian status												
Non-vegetarian	166	1.00	588	1.00	148	1.00	74	1.00	72	1.00	1,734	1.00
Vegetarian	62	1.49 (1.09, 2.03)	146	0.94 (0.77, 1.13)	35	0.90 (0.61, 1.33)	18	0.85 (0.49, 1.46)	16	1.23 (0.69, 2.17)	445	0.93 (0.83, 1.04)
P for heterogeneity		0.015		0.496		0.608		0.555		0.489		0.182
Diet group												
Meat eater	151	1.00	496	1.00	135	1.00	68	1.00	70	1.00	1,521	1.00
Fish eater	15	0.64 (0.37, 1.10)	92	1.02 (0.81, 1.29)	13	0.88 (0.49, 1.57)	6	0.43 (0.18, 1.01)	2	0.23 (0.06, 0.95)	213	0.83 (0.71, 0.96)
Vegetarian or vegan	62	1.39 (1.01, 1.91)	146	0.94 (0.77, 1.15)	35	0.89 (0.60, 1.32)	18	0.73 (0.42, 1.28)	16	1.08 (0.61, 1.91)	445	0.89 (0.80, 1.00)
P for heterogeneity		0.012		0.778		0.795		0.084		0.028		0.014

Author Conclusion:

- The overall cancer incidence rates of both the vegetarians and the non-vegetarians were low compared with national rates
- Within the study, the incidence of all cancers combined was lower among vegetarians than among meat eaters, but the incidence of colorectal cancer was higher in vegetarians than in meat eaters.

Reviewer Comments:

None.

Research Design and Implementation Criteria Checklist: Primary Research

Relevance Questions

1.	Would implementing the studied intervention or procedure (if found successful) result in improved outcomes for the patients/clients/population group? (Not Applicable for some epidemiological studies)	N/A
2.	Did the authors study an outcome (dependent variable) or topic that the patients/clients/population group would care about?	Yes
3.	Is the focus of the intervention or procedure (independent variable) or topic of study a common issue of concern to nutrition or dietetics practice?	Yes
4.	Is the intervention or procedure feasible? (NA for some epidemiological studies)	N/A

Validity Questions			
1.	**Was the research question clearly stated?**		Yes
	1.1.	Was (were) the specific intervention(s) or procedure(s) [independent variable(s)] identified?	Yes
	1.2.	Was (were) the outcome(s) [dependent variable(s)] clearly indicated?	Yes
	1.3.	Were the target population and setting specified?	Yes
2.	**Was the selection of study subjects/patients free from bias?**		Yes
	2.1.	Were inclusion/exclusion criteria specified (e.g., risk, point in disease progression, diagnostic or prognosis criteria), and with sufficient detail and without omitting criteria critical to the study?	Yes
	2.2.	Were criteria applied equally to all study groups?	Yes
	2.3.	Were health, demographics, and other characteristics of subjects described?	Yes
	2.4.	Were the subjects/patients a representative sample of the relevant population?	Yes
3.	**Were study groups comparable?**		Yes
	3.1.	Was the method of assigning subjects/patients to groups described and unbiased? (Method of randomization identified if RCT)	N/A
	3.2.	Were distribution of disease status, prognostic factors, and other factors (e.g., demographics) similar across study groups at baseline?	Yes
	3.3.	Were concurrent controls used? (Concurrent preferred over historical controls.)	Yes
	3.4.	If cohort study or cross-sectional study, were groups comparable on important confounding factors and/or were preexisting differences accounted for by using appropriate adjustments in statistical analysis?	Yes
	3.5.	If case control or cross-sectional study, were potential confounding factors comparable for cases and controls? (If case series or trial with subjects serving as own control, this criterion is not applicable. Criterion may not be applicable in some cross-sectional studies.)	Yes
	3.6.	If diagnostic test, was there an independent blind comparison with an appropriate reference standard (e.g., "gold standard")?	N/A
4.	**Was method of handling withdrawals described?**		N/A
	4.1.	Were follow-up methods described and the same for all groups?	N/A
	4.2.	Was the number, characteristics of withdrawals (i.e., dropouts, lost to follow up, attrition rate) and/or response rate (cross-sectional studies) described for each group? (Follow up goal for a strong study is 80%.)	N/A
	4.3.	Were all enrolled subjects/patients (in the original sample) accounted for?	N/A
	4.4.	Were reasons for withdrawals similar across groups?	N/A
	4.5.	If diagnostic test, was decision to perform reference test not dependent on results of test under study?	N/A
5.	**Was blinding used to prevent introduction of bias?**		Yes
	5.1.	In intervention study, were subjects, clinicians/practitioners, and investigators blinded to treatment group, as appropriate?	N/A
	5.2.	Were data collectors blinded for outcomes assessment? (If outcome is measured using an objective test, such as a lab value, this criterion is assumed to be met.)	N/A

	5.3.	In cohort study or cross-sectional study, were measurements of outcomes and risk factors blinded?	Yes
	5.4.	In case control study, was case definition explicit and case ascertainment not influenced by exposure status?	N/A
	5.5.	In diagnostic study, were test results blinded to patient history and other test results?	N/A
6.	**Were intervention/therapeutic regimens/exposure factor or procedure and any comparison(s) described in detail? Were interveningfactors described?**		Yes
	6.1.	In RCT or other intervention trial, were protocols described for all regimens studied?	N/A
	6.2.	In observational study, were interventions, study settings, and clinicians/provider described?	Yes
	6.3.	Was the intensity and duration of the intervention or exposure factor sufficient to produce a meaningful effect?	Yes
	6.4.	Was the amount of exposure and, if relevant, subject/patient compliance measured?	Yes
	6.5.	Were co-interventions (e.g., ancillary treatments, other therapies) described?	N/A
	6.6.	Were extra or unplanned treatments described?	N/A
	6.7.	Was the information for 6.4, 6.5, and 6.6 assessed the same way for all groups?	Yes
	6.8.	In diagnostic study, were details of test administration and replication sufficient?	N/A
7.	**Were outcomes clearly defined and the measurements valid and reliable?**		Yes
	7.1.	Were primary and secondary endpoints described and relevant to the question?	Yes
	7.2.	Were nutrition measures appropriate to question and outcomes of concern?	Yes
	7.3.	Was the period of follow-up long enough for important outcome(s) to occur?	Yes
	7.4.	Were the observations and measurements based on standard, valid, and reliable data collection instruments/tests/procedures?	Yes
	7.5.	Was the measurement of effect at an appropriate level of precision?	Yes
	7.6.	Were other factors accounted for (measured) that could affect outcomes?	Yes
	7.7.	Were the measurements conducted consistently across groups?	Yes
8.	**Was the statistical analysis appropriate for the study design and type of outcome indicators?**		Yes
	8.1.	Were statistical analyses adequately described and the results reported appropriately?	Yes
	8.2.	Were correct statistical tests used and assumptions of test not violated?	Yes
	8.3.	Were statistics reported with levels of significance and/or confidence intervals?	Yes
	8.4.	Was "intent to treat" analysis of outcomes done (and as appropriate, was there an analysis of outcomes for those maximally exposed or a dose-response analysis)?	N/A
	8.5.	Were adequate adjustments made for effects of confounding factors that might have affected the outcomes (e.g., multivariate analyses)?	Yes
	8.6.	Was clinical significance as well as statistical significance reported?	Yes
	8.7.	If negative findings, was a power calculation reported to address type 2 error?	N/A
9.	**Are conclusions supported by results with biases and limitations taken into consideration?**		Yes
	9.1.	Is there a discussion of findings?	Yes

	9.2.	Are biases and study limitations identified and discussed?	Yes
10.	**Is bias due to study's funding or sponsorship unlikely?**		Yes
	10.1.	Were sources of funding and investigators' affiliations described?	No
	10.2.	Was the study free from apparent conflict of interest?	Yes